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### Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims:

1. (previously presented) A method for making an infectious adenovirus having enhanced efficiency which comprises contacting a cell with or introducing into a cell:
  - (a) a first nucleic acid sequence encoding adenovirus sequences which, in the absence of intermolecular recombination, are incapable to encode an infectious, replicable or packageable adenovirus; and
  - (b) a second nucleic acid sequence encoding adenovirus sequences which, in the absence of adenoviral replication factors provided in trans or intermolecular recombination with said first nucleic acid sequence, are incapable to encode an infectious, replicable or packageable adenovirus;provided that said first and said second nucleic acid sequences each comprise a head-to-head ITR junction and said first nucleic acid and said second nucleic acid comprise recombinase recognition sites and wherein said first and said second nucleic acids are contacted with a recombinase which recognizes said first nucleic acid and said second nucleic acid recombinase recognition sites; whereby said first and said second nucleic acids recombine to form said infectious adenovirus.
2. (original) The method according to claim 1 wherein said first nucleic acid sequence is a plasmid containing a circularized adenovirus DNA molecule.
3. (previously presented) The method according to claim 2 wherein said plasmid includes a bacterial origin of DNA replication, an antibiotic resistance gene for selection in bacteria, a deletion or modification in E1 that renders the adenoviral sequences incapable to form

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- 1 infectious virus, or an expression cassette encoding a site-specific recombinase, and  
2 combinations thereof.
- 1 4 (original) The method according to claim 2 wherein said adenovirus DNA has a deletion  
2 of an adenoviral packaging signal, or wherein said packaging signal is flanked on either  
side by at least one site-specific recombinase recognition site.
- 1 5 (original) The method according to claim 4 wherein said adenovirus DNA comprises (i) a  
2 deletion of, (ii) a modification in, or (iii) sequences flanked with a site-specific  
3 recombinase recognition site, of an adenoviral gene selected from the group consisting of  
4 adenoviral E1 sequences extending beyond said packaging signal, adenoviral fibre gene  
5 sequences, adenoviral E3 gene sequences, adenoviral E4 gene sequences, and  
6 combinations thereof.
- 1 6 (original) The method according to claim 5 wherein said adenovirus DNA has a *lox* site  
2 located 5' of a pIX gene.
- 1 7 (currently amended) The method according to claim 2 wherein said plasmid is selected  
2 from the group consisting of pBHGloxΔE1,3, pBHG11lox, ~~pBHGΔE1,3lox~~, pBHGE3lox,  
3 pFG173lox, and pBHGloxΔE1,3Cre.
- 1 8 (original) The method according to claim 1 wherein said second nucleic acid sequence is  
2 a plasmid comprising:  
3 (a) said head-to-head ITR junction, and a packaging signal contained within the  
4 leftmost approximately 350 nt of the adenovirus genome;  
5 (b) a polycloning site or a foreign DNA or an expression cassette; and optionally,  
6 (c) a *lox P* site 3' of said polycloning site, foreign DNA, or expression cassette.

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9. (Currently amended) The method according to claim 8 wherein said plasmid is constructed by modification of a plasmid selected from the group consisting of pΔE1sp1Alox, pΔE1sp1AloxΔ, pΔE1sp1Blox, pΔE1sp1BloxΔ, ~~pMH4lox, pMH4loxΔ, pMH4loxΔlink, pCA13lox, pCA13loxΔ, pCA14lox, and pCA14loxΔ, pCA36lox, pCA36loxΔ, pCA36loxΔCreR, pCA36loxΔCreF, pCA35lox, pCA35loxΔCreITR, pDE111, pDE112, pDE113, pDE114, pDE115, pDE116, pDE117, and pDE118.~~

10. (previously presented) A recombinant adenovirus vector system comprising:

(a) a first nucleic acid sequence encoding adenovirus sequences which, in the absence of intermolecular recombination, are incapable to encode an infectious, replicable or packageable adenovirus, said first nucleic acid sequence comprising a head-to-head ITR junction and at least one site-specific recombinase recognition target site which is recognized by a site-specific recombinase; and,

(b) a second nucleic acid sequence encoding adenovirus sequences which, in the absence of adenoviral replication factors provided in trans or intermolecular recombination with said first nucleic acid sequence, are incapable to encode an infectious, replicable or packageable adenovirus, said second nucleic acid sequence comprising a head-to-head ITR junction and a site-specific recombinase recognition target site sufficiently identical with said recombinase recognition target site in said first nucleic acid as to be recognized by the same site-specific recombinase which recognizes said site-specific recombinase recognition target site in said first nucleic acid;

wherein said first and said second nucleic acid sequences, in combination and following site-specific intermolecular recombination, result in production of an infectious adenovirus, and wherein a site-specific recombinase which recognizes said site-specific recombinase recognition target sites either (i) is expressed by a cell into which said first and said second nucleic acids are introduced, (ii) is operatively encoded by said first

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nucleic acid, said second nucleic acid or both, or (iii) is provided in trans through expression from a third nucleic acid, or (iv) is provided in trans as an active protein.

11. (Currently amended) The recombinant adenovirus vector system of claim 10 comprising:

(a) a first nucleic acid sequence comprising a plasmid selected from the group consisting of pBHGloxΔE1,3, pBHG11lox, and pBHGloxΔE1,3Cre, and pBHGloxΔE1,3CreR; containing a circularized adenovirus DNA molecule and optionally including a bacterial origin of DNA replication and an antibiotic resistance gene for selection in bacteria and having a deletion or modification of the packaging signal, of additional E1 sequences, of E3, E4 or fibre, wherein said site-specific recombinase recognition target site is a *lox* P site located adjacent the pIX gene, E3, E4 or fibre of the virus, said plasmid optionally encoding Cre recombinase;

(b) a second nucleic acid sequence comprising a plasmid constructed by modification of a plasmid selected from the group consisting of pΔE1sp1Alox, pΔE1sp1AloxΔ, pΔE1sp1Blox, pΔE1sp1BloxΔ, pMH4lox, ~~pMH4loxΔ~~, pMH4loxΔlink, pCA13lox, pCA13loxΔ, pCA14lox, pCA14loxΔ, pCA36lox, pCA36loxΔ, pCA36loxΔCreR, pCA36loxΔCreF, pCA35lox, pCA35loxΔCreITR, pDC111, pDC112, pDC113, pDC114, pDC115, pDC116, pDC117, pDC118, and identifiable combinations thereof; and comprising:

- (i) ~~all or most of the left ITR and the packaging signal contained within the leftmost approximately 350 nt of the Ad genome or a head-to-head ITR junction;~~
- (ii) a polycloning site or a foreign DNA or an expression cassette; and,
- (iii) as said site-specific recombinase recognition target site, a *lox* P site 3' of said polycloning site or foreign DNA or expression cassette; and

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24 (c) a cell line that is normally able to support replication of adenovirus and which  
25 optionally expresses the recombinase Cre that is able to catalyze site-specific  
26 recombination between said *lox P* sites.

1 12. (original) The recombinant adenovirus vector system of claim 10 wherein said cell further  
2 expresses adenoviral E1.

1 13. (previously presented) The recombinant adenovirus vector system of claim 10 wherein  
2 said first nucleic acid sequence and said second nucleic acid sequence are cotransfected  
3 into said cell to produce an infectious virus vector comprising a left end, a polycloning  
4 site or a foreign DNA or an expression cassette from said second nucleic acid sequence,  
5 joined to a remaining portion of the adenoviral sequences from said first nucleic acid  
6 sequence.

1 14. (currently amended) The recombinant adenovirus vector system of claim 10 wherein said  
2 cell is co-transfected with a first nucleic acid sequence from a virus selected from the  
3 group consisting of AdLC8, AdLC8cluc, AdLC8cCE199, comprising a packaging signal  
4 flanked by *loxP* sites, and a second nucleic acid sequence comprising a packaging signal  
5 wherein said second nucleic acid sequence is constructed by modification of a plasmid  
6 selected from the group consisting of pΔE1sp1Alox, pΔE1sp1AloxΔ, pΔE1sp1Blox,  
7 pΔE1sp1BloxΔ, ~~pM114lox, pM114loxΔ, pM114loxΔlink, pCA13lox, pCA13loxΔ,~~

8 pCA14lox, and pCA14loxΔ, pCA36lox, pCA36loxΔ, pCA36loxΔCreR,

9 pCA36loxΔCreT, pCA35lox, pCA35loxΔCreIFR, pDC111, pDC112, pDC113, pDC114,

10 pDC115, pDC116, pDC117, pDC118, and identifiable combinations thereof; whereby

11 said *lox P* sites flanking said packaging signal of said first nucleic acid sequence are acted

12 upon by Cre recombinase expressed in said cells to induce excision of said packaging

13 signal, producing a noninfectious virus genome incapable of packaging its DNA into

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14 virions unless joined by Cre-mediated recombination to the *lox P* site of said second  
15 nucleic acid sequence to reconstitute a packaging signal therein.

1 15. (previously presented) The recombinant adenovirus vector system of claim 14 wherein,  
2 prior to said co-transfection, said first nucleic acid sequence is cleaved with a restriction  
3 enzyme that cuts between said *lox P* sites.

1 16. (previously presented) A kit for construction of recombinant adenovirus vectors  
2 comprising:

3 (A) a first nucleic acid sequence encoding adenovirus sequences which, in the absence  
4 of intermolecular recombination, are incapable to encode an infectious, replicable  
5 or packageable adenovirus, said first nucleic acid sequence comprising a head-to-  
6 head ITR junction and at least one site-specific recombinase recognition target site  
7 which is recognized by a site-specific recombinase;

8 (B) a second nucleic acid sequence encoding adenovirus sequences which, in the  
9 absence of adenoviral replication factors provided in trans or intermolecular  
10 recombination with said first nucleic acid sequence, are incapable to encode an  
11 infectious, replicable or packageable adenovirus, said second nucleic acid  
12 sequence comprising a head-to-head ITR junction and a site-specific recombinase  
13 recognition target site sufficiently identical with said recombinase recognition  
14 target site in said first nucleic acid as to be recognized by the same site-specific  
15 recombinase which recognizes said site-specific recombinase recognition target  
16 site in said first nucleic acid; and

17 (C) a cell wherein, when said component (a) and said component (b) are cotransfected  
18 and recombined through the action of a recombinase which recognizes said  
19 recombinase recognition sites, an infectious recombinant adenovirus vector is  
20 produced.

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2 17 (currently amended) The kit according to claim 16 wherein component (a) is selected  
3 from the group consisting of pBHGlox E1,3, pBHG11lox, ~~pBHGdX1Plox~~, pBHGE3lox,  
4 and pBHGlox E1,3Cre.

1 18 (currently amended) The kit according to claim 16 wherein said component (b) is  
2 constructed by modification of a plasmid selected from the group consisting of  
3 pΔE1sp1Alox, pΔE1sp1AloxΔ, pΔE1sp1Blox, and pΔE1sp1BloxΔ, ~~pMH4lox,~~

4 ~~pMH4loxΔ, pMH4loxΔlink, pCA13lox, pCA13loxΔ, pCA14lox, pCA14loxΔ,~~

5 ~~pCA36lox, pCA36loxΔ, pCA36loxΔCreR, pCA36loxΔCreT, pCA35lox,~~

6 ~~pCA35loxΔCreIFR, pDC111, pDC112, pDC113, pDC114, pDC115, pDC116, pDC117,~~

7 ~~pDC118, and identifiable combinations thereof.~~

1 19 (original) The kit according to claim 16 wherein said cell of (c) is selected from the group  
2 consisting of 293 cells, 293 cells expressing Cre, PER-C6 cells expressing Cre, 911 cells  
3 expressing Cre, and wherein said recombinase recognition sites are *lox P* sites.

1 20 (original) The recombinant adenovirus vector system according to claim 10 wherein an  
2 adenoviral gene mutation is rescued into said adenoviral vector recombinant.

1 21 (original) The recombinant adenovirus vector system according to claim 20 wherein said  
2 adenoviral gene mutation rescued into said adenoviral vector recombinant is a mutation in  
3 the adenoviral fibre gene, the adenoviral E4 gene, the adenoviral E3 gene, or  
4 combinations thereof.

1 22 (original) The recombinant adenovirus vector system according to claim 10 wherein said  
2 first nucleic acid sequence comprises a recombinase recognition site and a deletion in the  
3 adenoviral fibre gene.

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- 1 23 (original) The recombinant adenovirus vector system of claim 10 comprising:  
 2 (a) a first adenovirus vector having a fibre gene flanked by *loxP* sites;  
 3 (b) a plasmid comprising a bacterial origin of replication, a bacterial antibiotic resistance  
 4 marker, the right end of the Ad genome encompassing a fibre gene comprising a deletion,  
 5 a single *loxP* site located to the left of the fibre gene, and a foreign DNA insert between  
 6 the *loxP* site and the fibre gene.
- 1 24 (currently amended) An adenoviral vector selected from the group consisting of  
 2 pBHGloxΔE1,3, pBHG11lox, ~~pBHGdX1Plox~~, pBHGE3lox, pFG173lox, and  
 3 pBHGloxΔE1,3Cre.
- 1 25 (cancelled)
- 1 26 (original) A cell comprising the adenoviral vector of claim 24.
- 1 27 (cancelled)
- 1 28 (currently amended) A cell into which has been introduced a first vector selected from the  
 2 group consisting of pBHGloxΔE1,3, pBHG11lox, ~~pBHGdX1Plox~~, pBHGE3lox,  
 3 pFG173lox, and pBHGloxΔE1,3Cre, and a second vector constructed by modification of  
 4 a plasmid selected from the group consisting of pΔE1splAlox, pΔE1splAloxΔ,  
 5 pΔE1splBlox, pΔE1splBloxΔ, ~~pMH4lox~~, ~~pMH4loxΔ~~, ~~pMH4loxΔlink~~, pCA13lox,  
 6 pCA13loxΔ, pCA14lox, and pCA14loxΔ, and comprising a head-to-head ITR junction:  
 7 ~~pCA36lox~~, ~~pCA36loxΔ~~, ~~pCA36loxΔCreR~~, ~~pCA36loxΔCreT~~, ~~pCA35lox~~,  
 8 ~~pCA35loxΔCreITR~~, ~~pDE111~~, ~~pDE112~~, ~~pDE113~~, ~~pDE114~~, ~~pDE115~~, ~~pDE116~~, ~~pDE117~~,  
 9 ~~pDE118~~, and identifiable combinations thereof.



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29 (cancelled)

30. (cancelled)

31. (currently amended) A composition comprising the recombination product of a first vector selected from the group consisting of pBHGlox $\Delta$ E1,3, pBHG11lox, pBHGdX1Plox, pBHG E3lox, pFG173lox, pBHGlox $\Delta$ E1,3Cre, and a second vector constructed by modification of a plasmid selected from the group consisting of p $\Delta$ E1sp1Alox, p $\Delta$ E1sp1Alox $\Delta$ , p $\Delta$ E1sp1Blox, p $\Delta$ E1sp1Blox $\Delta$ , pMH4lox, pMH4lox $\Delta$ , pMH4lox $\Delta$ link, pCA13lox, pCA13lox $\Delta$ , pCA14lox, and pCA14lox $\Delta$ , and comprising a head-to-head ITR junction, pCA36lox, pCA36lox $\Delta$ , pCA36lox $\Delta$ CreR, pCA36lox $\Delta$ CreT, pCA35lox, pCA35lox $\Delta$ CreITR, pDC111, pDC112, pDC113, pDC114, pDC115, pDC116, pDC117, pDC118, and identifiable combinations thereof; wherein said first vector and said second vector are contacted optionally in the presence of Cre recombinase.

32. (original) The composition according to claim 31 wherein said first and said second vectors are contacted inside a cell and said recombination product is harvested from said cell.

33. (previously presented) An improved adenovirus vector system comprising two plasmids, neither of which alone comprises adenoviral sequences capable to produce infectious adenovirus when introduced into a cell but which, when both plasmids are introduced into a cell, recombine to form an infectious recombinant adenovirus, the improvement comprising: (a) inclusion of a head-to-head ITR junction in each of said two plasmids, and (b) inclusion, either in said first plasmid, said second plasmid, in both said first and said second plasmids or into a cell into which said first and said second plasmids are introduced, sequences to encode an active site-specific recombinase, and inclusion in said

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13 first and said second plasmid of recombinase recognition sequences, such that upon  
14 contact of said first and said second plasmids with said site-specific recombinase, site-  
15 specific recombination between said recombinase recognition sequences in said first  
16 plasmid and said second plasmid occurs.

1 34. (previously presented) A two-plasmid system for making an infectious adenoviral vector  
2 wherein each plasmid alone comprises adenoviral sequences incapable to encode an  
3 infectious adenoviral vector wherein, upon recombination, an infectious adenoviral vector  
4 is produced, provided that each plasmid of said two-plasmid system comprises (a) a head-  
5 to-head ITR junction; and (b) a recombinase recognition site such that upon contact of  
6 both plasmids of said two-plasmid system with a site-specific recombinase, site-specific  
7 recombination between the plasmids of said two-plasmid system occurs.